

REMARKS

Claims 1, 2 and 5-22 are pending.

Claim 17 was rejected under 35 U.S.C. § 112, second paragraph, on the untenable basis that "wherein said solid support is an essentially flat dish" in claim 2 fails to provide antecedent basis for "the cell dish support" in claim 17. Regardless, claim 17 as amended recites "the solid support," the antecedent for which is immediately apparent in "said solid support" in claim 2. This rejection should be withdrawn

Claims 1-4 and 12-16 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Wigstrom et al. (20040181343). Claims 5 and 17-20 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Wigstrom et al. in view of Knapp et al (U.S. 6,444,461). Claims 6-9 and 11-14 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Wigstrom et al. in view of Graves (U.S. 4,829,009) and further in view of Merkh et al. (U.S. 5,281,540). Claim 10 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Wigstrom et al. in view of Graves and Merkh et al. and further in view of Knapp et al.

Each of the foregoing rejections is premised on a fundamental misapprehension, if not disregard, of the plain and contrary teaching of Wigstrom, and should be withdrawn. Wigstrom fails to disclose either a mechanism or step for temporarily reducing the amount of liquid in a detection area in the course of the detection and any modification to Wigstrom to

provide that capability would be directly contrary to the express intentions stated in that reference. These rejections should be withdrawn.

Wigstrom discloses a microfluidic substrate having a plurality of parallel fluid microchannels opening to a chamber. Each microchannel delivers to the chamber a steady state fluid stream of either a test liquid or a buffer. A "sensor" in the form of one or more molecules is carried by a micropositioner. The microfluidic substrate and the micropositioner are movable relative to each other such that the sensor molecule can be scanned across each emerging fluid stream. These features of Wigstrom's device are plainly shown in Figures 10D and 10F of that reference, which are reproduced below:

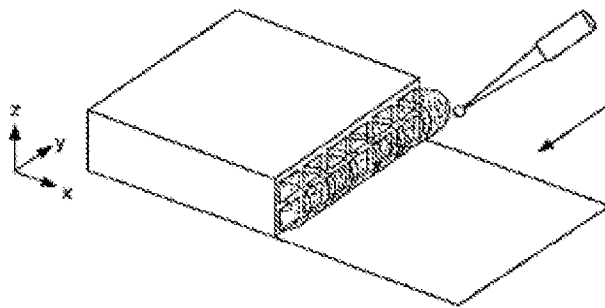


FIG. 10D

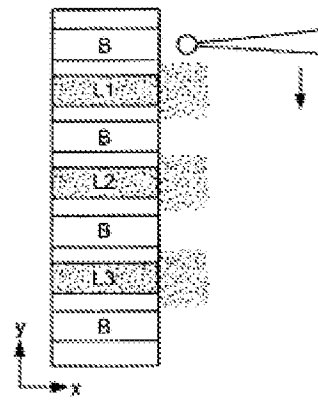


FIG. 10F

To provide for the necessary movement of the sensor across the emerging streams, Wigstrom teaches that the

microfluidic substrate may be moved in an x-, y-, and/or z-direction and may also be tilted. See Wigstrom at paragraph 89.

In contrast, the instant claims recite a mechanism adapted for (or step of) temporarily reducing the amount of liquid containing the second species in a detection zone during the detection. As the application plainly explains, this temporary reduction is beneficial for reducing the signal otherwise generated by the unbound ligand contained in the liquid, without requiring the complete removal of liquid or intermediate washing of the target species with a different liquid. See, e.g., page 5, lines 1-5, page 9, lines 13-24 and page 12, line 3 to page 13, line 27. Neither Wigstrom nor any of the secondary references relied upon by the Official Action mentions or enables this temporary reduction of fluid during a detection.

To attempt to cure that deficiency, the Official Action relies on Wigstrom's disclosure of "tilting" for the purpose of scanning a sensor across the plurality of fluid streams. However, any mechanism for tilting as disclosed by Wigstrom would necessarily preserve the steady flow of the emerging fluid streams. Accordingly, the tilting feature in Wigstrom plainly is not adapted for temporarily reducing fluid, much less reducing that fluid in the course of a detection.

Wigstrom requires that each fluid stream emerges "at the same rate" so as to establish "steady state concentrations."

(Paragraph 104). Thus, tilting Wigstrom's substrate would not temporarily reduce the amount of liquid in the detection area and Wigstrom explicitly teaches against that result. The Official Action fails to address this contrary requirement of Wigstrom.

The Official Action alternatively contends, relying on Graves and Merkh et al., that it would have been obvious to modify the tilting functionality in Wigstrom such that it eliminates fluid flow "for making a measurement without the sample/reagent being in contact with the portion to be detected (negative control)." See Official Action at page 6. The Official Action reiterates that contention at page 14, asserting that "the tilting of the device allows for removal of the materials for detection of the channel by itself in order to detect background noise . . ."

However, Wigstrom already provides a scheme for providing negative controls - each sample stream is separated by a buffer wash stream. Moreover, contrary to the reasoning stated in the Official Action, Wigstrom does not provide for *any* detection of the channels (detection is made only at the sensor species which is scanned across emerging fluid streams outside of the channels). The contention that it would be obvious to remove fluid from the channels for detection of the channel itself, given that Wigstrom does not disclose measuring *anything* in the channels, is nonsensical.

The measurement principle of Wigstrom is based on repeatedly substituted different liquids, such that equilibrium conditions for the detected complex would be repeatedly disrupted. The present invention, in contrast, is performed repeatedly in the same liquid, over a period of time and in a temporarily reduced amount, thereby preserving the equilibrium conditions for the complex.

Neither Wigstrom's intermediate wash streams nor the contrivance of the Official Action involving removing fluid from the channels even remotely satisfies the present recitations which enable a reference area and target area to be detected under the same fluid, not to mention that the amount of fluid is temporarily reduced during the detection.

Wigstrom, either alone or in combination with the cited secondary references, plainly lacks numerous other features that are recited in the claims of this application which are not even addressed in the Official Action.

For example, instant claim 1 recites a solid support "on which said first species can be attached in one or more non-overlapping defined areas thereon" and in which "at least one of the defined areas does not have said first species attached." These recitations are neither shown nor suggested by the very different structure (and purpose) of Wigstrom.

Wigstrom discloses a support (the microfluidic substrate) that is not adapted to have any target species

attached. Indeed, it is essential in Wigstrom that the species is not attached to the microfluidic substrate so that it may be scanned across the emerging fluid streams. The Official Action concedes this point at page 3 where it is acknowledged that "Wigstrom et al. further disclose a 'sensor chamber' which **receives** sensors."

Thus, Wigstrom fails to disclose a support on which a first species can be attached at one defined area and not attached at a different, reference area. None of the rejections set forth in the Official action even attempt to address this fundamental distinction of Wigstrom from the present claims.

New claims 21 and 22 further recite, respectively, "an aspirating device for aspirating liquid from said support before measurement, and for returning liquid to the support after measurement" and a "motor for enabling rotation of the dish at an angle deviating from the horizontal, so as to provide for a temporary reduction of the amount of liquid in said defined area of said support." These recitations are clearly absent from the prior art relied upon in the Official Action.

In view of the foregoing remarks, it is believed that the present application is in condition for allowance. Reconsideration and allowance are respectfully requested.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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